Office Action Summary	Application No.	Applicant(s)	
	09/763,957	BOTELLA MESA ET AL.	
	Examiner	Art Unit	
	MARIA B. MARVICH	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 April 2008 and 03 July 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1, 7, 9, 11-15, 19-24 and 26-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,7,9,11-15 and 19-24* is/are rejected.

7)☒ Claim(s) *26-35* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 April 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *6/24/08*.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 7, 9, 11-15, 19-24 and 26-35 are pending. This office action is in response to an amendment filed 4/29/08 and 7/3/08.

Claim Objections

In claim 1, 7, 9, 11-13, 15, 20 and 26-35, the claims have been amended to recite --confers or enhances the ability of operably linked sequences to be expressed upon induction-- as recommended in the office action mailed 11/29/07. Upon further consideration, it is recommended that the article "an" be inserted prior to "operably linked sequence".

The recitation in claim 1 step (ii) "residues of 2016 to 2384 of SEQ ID NO:3" should be amended to --residues 2016 to 2384 of SEQ ID NO:3--. Similar amendment to delete "of" should be made to claim 15 and newly added claims 26-35.

Finally, in claim1 and claim 15 following step (iv), the recitation "native form" should be amended to --native state--. The word form can mean "the visual appearance of something or someone", "visible shape or configuration" and "a way in which a thing exists or appears". Hence, it appears that by native form the form of the promoter itself is being described. The claim is attempting to describe the function of the native promoter, which is clearer described as native state.

In claim 7, the recitation, "structural gene or other nucleic acid obtainable by the method of isolating genomic DNA from plant cells, rendering the genomic DNA or portion thereof single stranded and then identifying a region on the genomic DNA which hybridizes to a primer" lacks clarity. 1) "The method" should be amended to --a method-- as use of the term "the" is

used when referring to limitations previously recited. In this case, the method of isolating genomic DNA has not been previously recited. 2) An article is required prior to "portion thereof". 3) Recitation of "identifying a region on a genomic DNA which hybridizes to a primer" does not indicate a step of hybridization. As well, "a genomic DNA" is more accurately described as, --a genomic DNA or a portion thereof--. Therefore, this recitation would be better if amended as, for example, --structural gene or other nucleic acid; wherein the promoter is obtainable by a method of isolating genomic DNA or a portion thereof from plant cells, rendering the genomic DNA or the portion thereof single-stranded and then hybridizing a primer to the genomic DNA or the portion thereof--.

It appears that claim 9 should be drawn to claim 1 or should be amended to be an independent claim as it recites a method of obtaining the isolated promoter of claim 7, however, the promoter of claim 7 has already been isolated by a method in which it is cloned and identified as either set forth in SEQ ID NO:3, a fragment comprising 2016-2384 or 95% identical thereof or a complement of any of these.

Claim 12 recites "a structural or regulatory gene" which should be amended to --a structural gene or a regulatory gene--. And for clarity the phrase, "the operably linked sequence comprising a structural gene or other nucleic acid" in claim 7 should be deleted. Otherwise an independent claim reciting--The genetic construct of claim 11, wherein the structural gene or other nucleic acid can is operably linked to said promoter--.

For accuracy and clarity, claim 13 should be amended to recite in line 3, --the plant--. In the reference in line 5 "said introduced structural or regulatory gene" to --the introduced structural gene or the introduced regulatory gene--. Similarly in the last line amendment should

be made to "said structural or regulatory gene". Applicant is reminded that when referencing a previous limitation is it proper to recite "the" or "said". However, when using said, the previous limitation is repeated verbatim. . A limitation recited using the article "a" or "an" refers to newly recited limitations. Additionally, the claim recites in the preamble "a method of altering a characteristic of a plant". The specification teaches that the plant is altered by introduction of a structural gene or other gene that alters the plant characteristic. The recitation that the gene "facilitates" the alteration does not clearly indicate the direct relationship between the altered characteristic and the introduced gene. Hence, line 4, --the structural gene or the regulatory gene alters the plant characteristic-- and the last line should be amended to recite --which then alters the plant characteristic--. In this way, the claim effect reflects the preamble.

Claim 20 should be amended to recite --A vegetative or a reproductive portion--.

Appropriate correction is required.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 7, 9, 11-15 and 19-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid sequence defining a promoter wherein the sequence is SEQ ID NO:3 or a fragment comprising nucleotides 2016-2384, does not reasonably provide enablement for any other embodiment. The specification

does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. **This rejection is maintained for reasons of record in the office action mailed 6/6/06 and 3/26/07. The rejection has been slightly reworded based upon applicants' amendment.**

1) Nature of invention. The invention is drawn to an isolated sequence that defines a promoter in which the promoter is said to direct expression of a gene encoding ACC synthase and is inducible in response to physical stimulation.

2) Scope of the invention. Applicants claim a genus of sequences that are nucleotide sequences that "define a promoter". Specifically, this genus comprises multiple sequences 1) a sequence of nucleotides having the sequence as set forth in SEQ ID NO:3, 2) a fragment comprising residues 2016 to 2384, 3) nucleotides with at least 95% identity to residues 2016-2384 of SEQ ID NO:3, 4) a sequence of nucleotides complementary to these sequences. Applicants recite a broad genus of sequences that appear to be functionally defined by being capable in their native form to direct expression of a gene encoding ACC synthase and that is further inducible. While it is presumed that the fragment must be able to encode an inducible promoter that can direct expression of a gene encoding ACC synthase, the specification does not provide adequate description in the specification of the required structural aspects of the sequences to provide this function. The structural requirements are further confused by reciting the sequences in terms of 95% identity or isolated following hybridization even at high stringency. Sequences with 95% identity have as many as 18 nucleotides altered. The fragment from 2016-2384 is functional as a whole as described by the specification and thus it is not known which 18 nucleotides can be altered without affecting activity. Hybridization detects

those sequences that have stretches of DNA in common. The result of this reaction need not comprise a promoter or promoter related sequences. For example, a sequence lacking sequences essential for promoter function can result in a nucleic acid sequence that is almost 100% related sequentially to regions of SEQ ID NO: 1 but has no relationship functionally.

3) Number of working examples and guidance. Functionally, applicants disclose that sequences that "define a promoter" "confers, activates or enhances expression of a structural gene or other nucleic acid in a plant cell" (see page 16, paragraph 5). Structurally, applicants disclose the sequence of pGEL-1 (SEQ ID NO:3). pGEL-1 comprises the promoter from mung bean ACC synthase that directs expression of a protein encoded by a sequence with 100% identity to SEQ ID NO: 1. Primer pairs 4 and 5 are used to isolate the promoter from mung bean. To characterize the promoter, applicants generate a series of seven serial deletions of the mung bean ACC synthase promoter region (page 36). A general decline in activity in the shorter promoters is detected in immature and mature leaf tissue but not evidently in any other tissues (page 37).

4) State of the art. The art does not disclose SEQ ID NO:3. Nor does the art or the specification teach the acc synthase promoter from mung bean or domains/ motifs required for promoter activity by the acc synthase promoter. Therefore, as neither domains nor structural motifs are available, the ability to identify

5) Unpredictability of the art. Applicants claim an isolated nucleic acid molecule that defines a promoter wherein the promoter in its native form directs expression of a gene encoding ACC synthase and is inducible in response to physical stimulation. However, applicants only disclose a single sequence that meets these functional limitations and that is SEQ ID NO:3.

Even the steps of claim 9, which are designed to isolate a promoter from native DNA will isolate a sequence corresponding to SEQ ID NO:3. By reciting sequences with 95% homology to residues 2016-2384 of SEQ ID NO:3 and by claiming sequences hybridizing under high stringency conditions, applicants recite a broad genus of promoters that can differ in any of 5% of the nucleotides of SEQ ID NO:3. In fact, 18 nucleotides can be altered in the functional fragment encompassing 2016-2384. Those nucleotides that can be altered cannot be surmised. As well, any nucleic acid that is isolated following hybridization at high stringency conditions requires only a small number of nucleic acids to match and the obtained nucleic acids may be very different from SEQ ID NO:1 such that the sequence obtained may actually encode a very different function. The relationship between the structure of the sequence and its function becomes unclear by claiming sequences that are isolated by relationship to SEQ ID NO:1 or by hybridization.

By disclosing pGEL-1, the applicants have not reduced to practice the claimed invention. Applicants have not demonstrated a representative number of sequences that comprise relevant identifying characteristics, specific features or functional attributes that would distinguish different members of the claimed genus. In other words, a number of sequences fit into this broad genus of sequences that can potentially be isolated but the skilled artisan cannot envision the detailed structure of the broad class of sequences that are in their native form capable of directing expression of ACC synthase and are inducible given the lack of adequate description of structural requirements. Because applicants do not provide the structural requirements of the sequences of the fragment of SEQ ID NO:3 that "confers, activates or enhances expression of a structural gene or other nucleic acid in a plant cell", deviation from the entire sequence of

nucleotides of pGEL-1 that can perform the same function are not known. Nor can the sequences that cannot be altered or cannot be deviated from cannot be guessed. Isolation of a promoter from such sequences requires a detailed understanding of the structural requirements of the promoter. Applicants' disclosure has amounted to a statement that the protein is part of the invention and a reference to a potential method for isolating it, by sequence identity. It would require undue experimentation to identify those molecules that are 95% identical to SEQ ID NO:3.

6) Amount of Experimentation Required. The specification provides a single reference sequences without identifying relevant characteristics or structural-functional relationships. Thus neither the specification nor the prior art teach the structural requirements of sequences with at least 95% similarity to residues 2016-2384 of SEQ ID NO:3 or a complement of these sequences. Given the large size and diversity of the recited sequences, the absence of disclosed or art recognized correlations between structure and function and the large number of potential sequences or homologs, it must be considered that any sequence with promoter activity in a plant cell must be empirically determined.

Response to Argument

Applicants' arguments filed 7/3/08 have been fully considered but they are not persuasive. Applicants argue promoter elements are flexible and point mutations do not normally alter the expression intensity or pattern of expression promoters and it would be routine to assay or identify functional variants of SEQ ID NO:3. However, while the specification teaches that SEQ ID NO:3 and particularly fragments from 2016, 1773, 1601, 1357, 1189 and

819 to 2384 have promoter activity, the specification does not teach what modifications can be made to any of these fragments such that promoter activity is retained. This is not a question of undue experimentation because absent structural guidance, no amount of modification would *a priori* allow one to modify the promoter 5% and know what sequences cannot be modified. Applicants argue that a promoter is afforded flexibility that is not afforded modification of a protein. However, promoter sequences comprise critical regions and nucleotides that cannot be modified and applicants have no provided this guidance in the specification. To identify these sequences at this point would be an inventive step that is not supported by the guidance in the specification. In other words, the specification does not provide the teachings that would lead one to those regions or nucleotides that are critical within these fragments. Hence the structural requirements of the desired promoters are vitually unknown and undue experimentation would be required to assess the potentially functionally diverse population of seqeunces with 95% homology. Sequences with 95% homology can have as many as 18 residues altered and in any number of combinations and assessing each of these given the lack of guidance in the specification amounts to undue experimentation.

Conclusion

Claims 1, 7, 9, 11-15 and 19-24 are rejected.

Claims 26-35 are objected to.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARIA B. MARVICH whose telephone number is (571)272-0774. The examiner can normally be reached on M-F (7:00-4:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, PhD can be reached on (571)-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maria B Marvich, PhD
Primary Examiner
Art Unit 1633

/Maria B Marvich, PhD/
Primary Examiner, Art Unit 1633